



**Billing Code: 4160-90-P**

**DEPARTMENT OF HEALTH AND HUMAN SERVICES**  
**Agency for Healthcare Research and Quality**

**Scientific Information Request on Radiotherapy Treatments for  
Head and Neck Cancer**

**AGENCY:** Agency for Healthcare Research and Quality (AHRQ), HHS.

**ACTION:** Request for Scientific Information Submissions.

**SUMMARY:** The Agency for Healthcare Research and Quality (AHRQ) is seeking scientific information submissions from the public on 3-Dimensional Conformal Radiotherapy (3DRT), Intensity-Modulated Radiotherapy (IMRT), Stereotactic Body Radiotherapy (SBRT), and Proton Beam Radiotherapy (PBRT). Scientific information is being solicited to inform our update review of *Radiotherapy Treatments for Head and Neck Cancer*, which is currently being conducted by the Evidence-based Practice Centers for the AHRQ Effective Health Care Program. Access to published and unpublished pertinent scientific information on 3-Dimensional Conformal Radiotherapy (3DRT), Intensity-Modulated Radiotherapy (IMRT), Stereotactic Body Radiotherapy (SBRT), and Proton Beam Radiotherapy (PBRT) will improve the quality of this review. AHRQ is conducting this comparative effectiveness review pursuant to Section 1013 of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Public Law 108-173, and Section 902(a) of the Public Health Service Act, 42 U.S.C. 299a(a).

**DATES:** *Submission Deadline* on or before [INSERT DATE 30 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].

**ADDRESSES:**

*Online submissions:* <http://effectivehealthcare.AHRQ.gov/index.cfm/submit-scientific-information-packets/>. Please select the study for which you are submitting information from the list to upload your documents.

*E-mail submissions:* SIPS@epc-src.org.

*Print submissions:*

Mailing Address:

Portland VA Research Foundation

Scientific Resource Center

ATTN: Scientific Information Packet Coordinator

PO Box 69539

Portland, OR 97239

Shipping Address (FedEx, UPS, etc.):

Portland VA Research Foundation

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3710 SW U.S. Veterans Hospital Road

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**FOR FURTHER INFORMATION CONTACT:**

Robin Paynter, Research Librarian, Telephone: 503-220-8262 ext. 58652  
or Email: SIPS@epc-src.org.

## SUPPLEMENTARY INFORMATION:

The Agency for Healthcare Research and Quality has commissioned the Effective Health Care (EHC) Program Evidence-based Practice Centers to complete an updated review of the evidence for *Radiotherapy Treatments for Head and Neck Cancer*.

The EHC Program is dedicated to identifying as many studies as possible that are relevant to the questions for each of its reviews. In order to do so, we are supplementing the usual manual and electronic database searches of the literature by requesting information from the public (e.g., details of studies conducted). We are looking for studies that report on *Radiotherapy Treatments for Head and Neck Cancer*, including those that describe adverse events. The entire research protocol, including the key questions, is also available online at:

<http://effectivehealthcare.AHRQ.gov/ehc/products/569/1852/head-neck-cancer-update-140204.pdf>

This notice is to notify the public that the EHC program would find the following information on 3-Dimensional Conformal Radiotherapy (3DRT), Intensity-Modulated Radiotherapy (IMRT), Stereotactic Body Radiotherapy (SBRT), and Proton Beam Radiotherapy (PBRT) helpful:

- A list of completed studies your company has sponsored for this indication. In the list, *indicate whether results are available on ClinicalTrials.gov along with the ClinicalTrials.gov trial number.*
- *For completed studies that do not have results on ClinicalTrials.gov, a summary, including the following elements: study number, study period, design, methodology, indication*

and diagnosis, proper use instructions, inclusion and exclusion criteria, primary and secondary outcomes, baseline characteristics, number of patients screened /eligible /enrolled /lost to follow-up /withdrawn /analyzed, effectiveness/efficacy, and safety results.

- *A list of ongoing studies your company has sponsored for this indication.* In the list, please provide the ClinicalTrials.gov trial number or, if the trial is not registered, the protocol for the study including a study number, the study period, design, methodology, indication and diagnosis, proper use instructions, inclusion and exclusion criteria, and primary and secondary outcomes.
- Description of whether the above studies constitute *ALL Phase II and above clinical trials* sponsored by your company for this indication and an index outlining the relevant information in each submitted file.

Your contribution is very beneficial to the Program. The contents of all submissions will be made available to the public upon request. Materials submitted must be publicly available or can be made public. Materials that are considered confidential; marketing materials; study types not included in the review; or information on indications not included in the review cannot be used by the Effective Health Care Program. This is a voluntary request for information, and all costs for complying with this request must be borne by the submitter.

The draft of this review will be posted on AHRQ's EHC program website and available for public comment for a period of 4 weeks. If you would like to be

notified when the draft is posted, please sign up for the e-mail list at:  
<http://effectivehealthcare.AHRQ.gov/index.cfm/join-the-email-list1/>.

*The systematic review will answer the following questions. This information is provided as background. AHRQ is not requesting that the public provide answers to these questions.* The entire research protocol, is also available online at:

<http://effectivehealthcare.AHRQ.gov/ehc/products/569/1852/head-neck-cancer-update-140204.pdf>

## KEY QUESTIONS (KQs)

### *Key Question 1*

What is the comparative effectiveness of 3DRT, IMRT, SBRT, and PBRT regarding adverse events and quality of life (QoL)?

### *Key Question 2*

What is the comparative effectiveness of 3DRT, IMRT, SBRT, and PBRT regarding tumor control and patient survival?

### *Key Question 3*

Are there differences in comparative effectiveness of 3DRT, IMRT, SBRT, and PBRT for specific patient and tumor characteristics?

### *Key Question 4*

Is there variation in comparative effectiveness of 3DRT, IMRT, SBRT, and PBRT because of differences in user experience, treatment planning, treatment delivery, and target volume delineation?

PICOTS (Population, Intervention, Comparator(s), Outcomes, Timing, Setting)

Identify for each key question:

*Population(s)*

KQs 1-4: Populations of interest include patients with head and neck cancer. To define what constitutes head and neck cancer, we consulted clinical resources such as the National Cancer Institute's Physician Data Query (PDQ) Cancer Information Summary and the National Comprehensive Cancer Network. The consensus definition of head and neck cancer includes tumors of:

1. larynx
2. pharynx (hypopharynx, oropharynx and nasopharynx)
3. lip and oral cavity
4. paranasal sinus and nasal cavity
5. salivary gland
6. occult primary of the head and neck

The following tumors are excluded:

1. brain tumors
2. skull base tumors
3. uveal/choroidal melanoma, other ocular and eyelid tumors
4. otologic tumors
5. cutaneous tumors of the head and neck (including melanoma)
6. thyroid cancer
7. parathyroid cancer
8. esophageal cancer

## 9. trachea tumors

All therapeutic strategies will be included. Radiotherapy (RT) can be delivered as primary (curative) intent therapy or as an adjunct to surgery. Chemotherapy can also be given as an adjunct to radiation therapy, particularly in patients with more advanced cancer (i.e., stages III or IV). We will seek direct evidence for one intervention compared to another, with or without chemotherapy or surgery.

### *Interventions*

The primary interventions of interest in all therapeutic settings are:

1. 3 dimensional conformal radiotherapy (3DRT): defined as any treatment plan where CT-based forward treatment planning is used to delineate radiation beams and target volumes in three dimensions
2. intensity modulated radiotherapy (IMRT): defined as any treatment plan where intensity-modulated radiation beams and computerized inverse treatment planning is used
3. stereotactic body radiation therapy (SBRT): defined as conformal RT (forward or reverse-planned) delivered in 3 to 5 relatively larger doses of ionizing radiation than typically delivered in a standard conformal schedule of 25-35 doses
4. proton beam radiotherapy (PBRT): defined as any treatment plan where proton beam radiation is used

Interventions may occur as part of a multimodal treatment strategy if the comparisons only differ with respect to the radiation therapy given.

## *Comparators*

All therapies will be compared to each other as part of a continuum of treatment for patients with head and neck cancer. Thus, we will include studies in which a RT method was compared to a different method, for example with or without chemotherapy or surgery. We will include all studies from which we can be reasonably certain additional treatments are contemporary and similar, leaving the major comparison that between RT modalities; those that we cannot ascertain from the publication will be excluded. To ensure chemotherapy or other treatments are similar and contemporary, we will consult accepted guidelines such as those from the National Comprehensive Cancer Network (NCCN) or National Cancer Institute (NCI). We will not extract details on chemotherapy dosages or schedules, but rather will ascertain their degree of general similarity and the proportions of patients who receive and complete such regimens. We will categorize and synthesize evidence according to overall treatment, for example concurrent chemoradiotherapy, or adjuvant radiotherapy, not mixing these in the strength of evidence synthesis.

## *Outcomes*

KQ 1, 3 & 4:

1. Final outcomes: quality of life (QoL) and adverse events including; radiation induced toxicities, xerostomia, mucositis, taste changes, dental problems, and dysphagia.
2. Intermediate outcomes: Salivary flow, probability of completing treatment according to protocol.



We will search for evidence related to user experience, treatment planning, and target volume delineation within the context of KQ4. In the absence of an evidence-base on these measures, these issues will be addressed as appropriate in both the future research needs and discussion sections of the report.

Based on input received from the TEP, any outcomes not adequately addressed in the literature will be stated as evidence gaps for primary research in the future research needs section of the report.

KQ 2, 3 & 4:

1. Final outcomes: Overall survival and cancer specific survival
2. Intermediate outcomes: Local control, and time to recurrence

### *Timing*

All durations of follow-up will be considered

### *Settings*

Inpatient and outpatient

**Dated: March 6, 2014.**

Richard Kronick,  
AHRQ Director.

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